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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,250	11/26/2003	Thomas M. DiMauro	3518.1024-000	6059

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EXAMINER	
MAEWALL, SNIGDHA	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,250	DIMAURO ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-10,21-25,27-30,60,70,89,91 and 92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-10,21-25,27-30,60,70,89,91 and 92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/02/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Receipt of Applicants' arguments /remarks, IDS, amended claims and **RCE** filed on 03/02/09 is acknowledged.

Claims **6-7, 26 and 57-58** have been canceled. Claims **11-20, 31-56, 59, 61-69, 71-88** and **90** have been withdrawn.

New claim **92** has been added in this application.

Accordingly, claims **1-5, 8-10, 21-25, 27-30, 60, 70, 89 and 91-92** are being examined on the merits herein.

The rejections made in the previous office action dated 09/02/08 have been withdrawn in view of Applicant's amendments to the claims.

The following new rejections are necessitated by claim amendments.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-3, 5, 8-10, 21-23, 25, 27-30, 70, 89 and 91-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cullis Hill (USP 6,593,310) in view of Tobinick US Patent Application Publication US 20010026801 (4 October 2001) and further in view of Radomsky (US 5,942,499).

Radomsky teaches a bone growth-promoting composition comprising growth factors such as fibroblast growth factor and platelet-derived growth factor and their methods of use (column 1, lines 19, 35-36, and 61). The invention can be used in various sites of desired bone growth including vertebral compression fractures and in pathological bone defects associated with osteoporosis (column 2, lines 50 and 55-58). The invention describes an injectable mixture of growth factor for intraosseous, or within bone, administration (column 12, lines 5-12).

The reference does not teach administration of anti-resorptive agent.

Cullis teaches a method of treating osteoporosis comprising administering to a mammal a compound such as pentason polysulfate (abstract).The reference teaches that estrogen is known to reduce fractures and is an example of an anti-resorptive agent. (See column 1, lines 59-60). The reference teaches that in the process of treating osteoporosis an effective amount of polysulfated polysaccharide for instance calcium pentosan polysulfate can be given and optionally with the compounds such as fosamax, estrogen, calcium supplements, calcitrol etc (see column 4,lines 40-50).

While Cullis teaches agents to treat osteoporosis, Cullis patent does not teach anti-resorptive agent such as infliximab.

The '801 publication teaches compositions comprising cytokine antagonists, including etanercept or infliximab in combination with a second therapeutic agent (paragraphs 6, 14, 18, 25,48, and 78). Routine dose optimization and dosing intervals are taught at paragraphs 87-94 and include ranges of 0. l mg to 300mg per dose depending on the route of administration (compare instant claim 11).

Radomsky teaches administration of growth factors to bone. Radomsky teaches a bone growth-promoting composition comprising growth factors such as fibroblast growth factor and platelet-derived growth factor and their methods of use (column 1, lines 19, 35-36, and 61). The invention can be used in various sites of desired bone growth including vertebral compression fractures and in pathological bone defects associated with osteoporosis (column 2, lines 50 and 55-58). The invention describes an injectable mixture of growth factor for intraosseous, or within bone, administration (column 12, lines 5-12).

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ....[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted).

In view of the facts recited above, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to combine the prior art elements according to known methods to yield predictable results. The prior art teaches all of the limitations of the claimed invention. Cullis teaches treatment of

osteoporosis with antiresoptive agent and/or in combination with other actives involved in treatment of osteoporosis and the ‘801 teaches the species of infliximab and etanercept for the same purpose in combinatorial composition. The person of ordinary skill in the art would have been motivated to combine the references because both references teach combinatorial compositions comprising anti-TNF agents or osteoporosis treating agents. The person of ordinary skill would have reasonably expected success because the combinatorial compositions comprising cytokine antagonists and other active agents which help in treating osteoporosis were well known in the art at the time of the instant invention, as evidenced by the 'Cullis patent and one of skill in the art would have expected success by substituting the species of infliximab as taught by the '801 patent with the anti-TNF agents taught by the Cullis patent. The person of ordinary skill in the art could have combined the elements as claimed by known methods to produce a composition comprising infliximab and bone forming agents. One of skill in the art would have recognized that the results of the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time the invention was made, as demonstrated by the teachings of the Cullis patent and 801 publication. Further, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ...[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations’ omitted).

It would have been further obvious to one of ordinary skill in the art to administer the formulations into the bone motivated by the teachings of Radomsky et al. with a reasonable expectation of success.

4. Claims 4 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cullis Hill (USP 6,593,310) in view of Tobinick US Patent Application Publication US 20010026801 (4 October 2001) and further in view of Radomsky (US 5,942,499) and further in view of Boyle et al. (US 2003/0207827).

The references discussed above do not teach patient as post menopausal.

Boyle et al. teach methods to treat bone diseases such as osteoporosis comprising osteoprotegrin, which is a polypeptide that plays a role in promoting bone accumulation (page 1, paragraphs [0001] and [0006]). Boyle et al. further teach treatment of osteoporosis in postmenopausal women and a direct relationship between osteoporosis and incidence of hip and neck fractures (page 9, paragraph [0095]). Osteoprotegrin acts as a receptor of the TNF family and prevents receptor-ligand interaction (page 4, paragraph [0043]). Osteoprotegrin also blocks interleukin (IL)1-α and IL1-β produced hypercalcemia (page 40, paragraph [0344]). Boyle et al. also teaches that estrogen is a known anti-resorptive agent (page 41, paragraph [0355]).

It would have been obvious to one of ordinary skill in the art at the time of instant invention to utilize the bone forming agent and infliximab to post menopausal women as

a patient motivated by the teachings of Boyle et al. teaching the administration of antiresoptive agents for treatment of osteoporosis in post menopausal women.

5. Claim 60 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cullis Hill (USP 6,593,310) in view of Tobinick US Patent Application Publication US 20010026801 (4 October 2001) and further in view of Trieu et al. ((US 2002/0026244).

The references discussed above do not teach implants.

Trieu teaches methods of implanting nucleus pulposus implants (page 1, paragraph [0007]). The method involves removal of the natural nucleus pulposus of the intravertebral disc and implantation of the nucleus pulposus of the invention (page 10, paragraph [0109]). The nucleus pulposus implant of the invention may contain pharmacological agents used to treat osteoporosis including a bone morphogenetic protein, growth factors such as fibroblast growth factor and platelet-derived growth factor, and steroids (page 9, paragraphs [0101] and [0104]). The device of Trieu is placed adjacent to unfractured bones (page 9, paragraphs [0104]). Since the nucleus pulposus implant of the invention may contain pharmacological agents used to treat osteoporosis including a bone morphogenetic protein (see page 9, paragraph [0101]), it would be obvious that the device can be used to treat fractured bones such as a hip bone. Thus Trieu teaches local administration in between bones.

It would have been obvious to the one of ordinary skilled in the art at the time the invention was made to incorporate highly specific cytokine antagonist such as infliximab as taught by '801 to the teachings of Trieu since the reference teaches advantage of the

same in treating osteoporosis with pharmacologivla gents such as bone morphogenetic protein etc. One skilled in the art would have been motivated to administer in o the bone the formulation comprising the bone forming agent and infliximab because Trieu et al. successfully teach local administration of implants/drug in between bones in order to treat osteoporosis.

Response to Arguments

6. Applicant's arguments with respect to claims **1-5, 8-10, 21-25, 27-30, 60, 70, 89 and 91-92** have been considered but are moot in view of the new ground(s) of rejection.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/

Examiner, Art Unit 1612

/Gollamudi S Kishore /

Primary Examiner, Art Unit 1612